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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,633	07/10/2001	Robert John Macleod Wilson	117-347	5975

23117 7590 06/17/2003

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EXAMINER

ANGELL, JON E

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 06/17/2003

26

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Paper No. 26

Application Number: 09/787,633
Filing Date: July 10, 2001
Appellant(s): WILSON ET AL.

B.J. Sadoff
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 3/26/03.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

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(7) *Grouping of Claims*

Appellant's brief includes a statement that claims 12 and 13 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) *Grounds of Rejection*

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph. This rejection is set forth in prior Office Action, Paper No. 17.

The following ground(s) of rejection (set forth in prior Office Action, Paper No. 17) are applicable to the appealed claims:

Claim Rejections - 35 USC § 112, first paragraph

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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2. Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 12 and 13 are reproduced for convenience below:

12. A method for screening for a compound that inhibits the growth of an organism comprising the ycf24 gene, the method comprising

(i) contacting a test compound with the ycf24 gene product, and

(ii) determining whether the test compound inhibits the activity of or binds to the product, any such binding or inhibition suggesting that the compound may inhibit the growth of the organism.

13. The method according to claim 12 in which the organism is a malaria parasite.

The instant claims encompass a method comprising contacting a test compound with the ycf24 gene product and determining if the test compound either 1) inhibits the activity of the ycf24 gene product, or 2) binds to the ycf24 gene product. The claims indicate that if the test compound either binds to the ycf24 gene product or inhibits the activity of the ycf24 gene product, then the test compound may be an inhibitor of the growth of an organism which comprises the ycf24 gene.

The specification explicitly discloses three different ycf24 genes, each from a different microbial organism. Specifically, the nucleotide sequence of the ycf24 gene of *Plasmodium*

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falciparum is disclosed as the sequence of SEQ ID NO: 1, the nucleotide sequence of the *ycf24* gene of *Synechocystis Sp* strain PCC6803 is disclosed as the sequence of SEQ ID NO: 2, and the nucleotide sequence of the *ycf24* gene of *E. coli* is disclosed as the sequence of SEQ ID NO: 3 (see page 6, lines 9-12). It is pointed out that claim 12 specifically indicates in step (i) that a test compound is contacted with **the ycf24 gene product**. Considering the specification discloses three different *ycf24* genes, the Examiner looked to the specification for a definition of the term “*ycf24* gene product” in order to determine the metes and bounds of the claim. The specification defines the term “*ycf24* gene product” by stating,

“The *ycf 24* gene product is generally one which can be expressed from the coding region of: (a) the polynucleotide sequence of SEQ ID NO: 1, 2 or 3 or a fragment thereof; or (b) polynucleotides which can selectively hybridize to the coding region of (a) of (sic) a fragment thereof; or (c) polynucleotides which, but for the degeneracy of the genetic code, would hybridise to (a) or (b).” (See page 4, line 32 through page 5, line 5); and

“The *ycf 24* gene product generally has at least 50% sequence identity to the amino acid sequence shown is (sic) SEQ ID NO: 1, 2 or 3, preferably at least 80 or 90% and more preferably at least 95, 97 or 99% over a region of at least 20, preferably at least 30, for instance at least 46, 60 100 or more contiguous amino acids. The term *ycf 24* product includes fragments of the amino acid sequences of SEQ ID NO: 1, 2 or 3 or of the homologous sequences discussed above.” (See page 5, lines 17-25).

Using the specification to define the term “*ycf24* gene product”, the claims clearly encompass a method using the *ycf24* gene product, wherein the *ycf24* gene product can be any amino acid sequence that generally are at least 50% identical to the amino acid sequence encoded by SEQ ID NO: 1, 2 or 3, and includes fragments thereof. Therefore, the claims encompass a huge number of different possible “*ycf2* gene products”, considering every possible amino acid sequence that “generally has at least 50% sequence identity” to the amino acid sequence encoded by SEQ ID NO: 1, 2 or 3, and fragments thereof.

Although the claims encompass a genus of ycf24 gene products comprising a huge number of different possible species, the specification only explicitly discloses three members of this huge genus: the ycf24 gene products of *Plasmodium falciparum*, *Synechocystis Sp* strain PCC6803, and *E. coli* (see SEQ ID NO: 1, 2 and 3, respectively). Therefore, the claims clearly encompass sequences whose structures are not explicitly disclosed in the instant specification.

The written description guidelines note regarding such genus/species situations, “Satisfactory disclosure of a ‘representative number’ depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.” (Emphasis added by the Examiner for clarity; See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Therefore, in order to satisfy the written description requirement, the necessary common attributes or features possessed by all “ycf24 gene products” (as defined by the specification) must be described. The description would have to include a indication of the particular sequences within ycf24 that which are critical for ycf24 function. In the instant case, the necessary common attributes or elements possessed by all ycf24 gene products are not disclosed. No structural limitations or requirements which provide guidance on the identification of the particular sequences critical for ycf24 function is provided. There is no disclosure indicating which sequences that “generally have at least 50% sequence identity” to the amino acid sequences encoded by SEQ ID NO: 1, 2 or 3 would have growth-associated functions. Without a clear disclosure indicating the attributes/elements critical for yf24 function, one of skill in the art would not readily recognize which sequences encompassed by the claims were functional and which were not functional.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that:

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“In claims to genetic material, however, a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA,” without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. (Emphasis added by Examiner) One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does “little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.”). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. “

In the instant case, the generic definition of the term “ycf24 gene product”, which encompasses ycf24 gene products from different species of organisms, does not distinguish the claimed genus from others. The specification does not define any structural features which are commonly possessed by all ycf24 gene products that distinguish them from others.

It is noted that in *Fiers v. Sugano* (25 USPQ2d, 1601), the Fed. Cir. concluded that “...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after the gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility.”

In the instant case, only three specific ycf24 gene products (those corresponding to SEQ ID NO: 1-3) are described in the specification as having growth-related functions. There is no evidence that any other species encompassed by the claims would have the same function as the three explicitly described species.

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Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that: "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of the invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of sequences other than those expressly disclosed which have the desired function (i.e. growth-related function) and which would be functional in a screening assay to identify compounds that inhibit the growth of an organism. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not adequately described in the specification.

(11) Response to Argument

Introduction:

The claimed invention is drawn to a method of screening for a compound that inhibits the growth of an organism comprising the ycf24 gene, the method comprising (i) contacting a test compound with the ycf24 gene product, and (ii) determining whether the test compound inhibits the activity of or binds to the product, any such binding or inhibition suggesting that the compound may inhibit the growth of the organism. Claim 13 limits the method of claim 12 such that the organism can only be a malaria parasite (i.e. any malaria parasite).

It is respectfully pointed out that the claimed invention is very broad and encompasses a method for screening for a compound that inhibits the growth of any organism comprising the ycf24 gene.

Although the Appellant's statement regarding the issues in the brief is correct, it is respectfully pointed out that the issue is not merely whether one of skill in the art could recognize the structure of any ycf24 gene product encompassed by the claim; but rather, does the specification adequately describe the necessary common attributes and elements possessed by all members of the genus. It is the Examiner's position that the specification does not adequately describe the necessary common attributes and elements possessed by all members of the genus of ycf24 gene products encompassed by the claims.

It is pointed out that it is essential to the claimed method that all "ycf24 gene products" have a growth-associated function. That is, in order for the method to work, all ycf24 gene products encompassed by the claims must be involved in the growth of the organism. Therefore, the specification must adequately describe the necessary common attributes and elements possessed by all members of the genus such that one of skill in the art could identify functional ycf24 gene products. It is noted that the specification discloses, "The high level of conservation of ycf24 (~50% amino acid identity of the putative encoded peptide product with other orthologues) suggests that it is under strong selective pressure and likely to have a general function." (Emphasis added by the Examiner; See paragraph bridging pages 1-2 of the specification). This statement indicates that the only criterion used to conclude that all ycf24 gene products have similar function is sequence similarity (i.e. sequence homology). However, sequence similarity (i.e. sequence homology) is a very unreliable predictor of gene function. For instance, it is well known that the disease sickle cell anemia is caused by a single nucleic acid change in the beta-globin gene which alters the gene product (hemoglobin) and leads to the

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disease. Therefore, even gene products which differ by only a single sequence change can have different functions.

The ycf24 genes:

The Appellant argues in the Appeal Brief filed 3/26/03 that the specification contains a written description of the claimed invention. The Appellant refers to five literature references that describe ycf24 genes (submitted with the Response of October 25, 2002). The Appellant argues that the five literature references provide a description of ycf24 gene sequences from five different organisms, which demonstrates that persons skilled in the art consider the term “ycf24 gene” to be clear enough to be used in published scientific articles. Appellants also contend that said references show that the “ycf24 gene” has a highly conserved sequence across species, that this sequence has allowed persons skilled in the art to recognize the gene in a variety of genomes, and that the ycf24 gene could be easily identified in the genome of any new species.

In response, it is acknowledged that the five cited references refer to genes of different species of organisms wherein the genes have been named “ycf24”. However, it appears that all of the genes have been named “ycf24” based solely on sequence similarity. For example, Kowallik (one of the five references cited by the Appellant) teaches, “Open reading frames shared by homologous sequences of other chloroplast genomes are designated as ycf” (see Kowallik p. 342, lines 4-5) indicating that the term “ycf” was assigned based on sequence similarity. Douglas (also cited by Appellant) teaches that ycf’s are “hypothetical chloroplast frames” (see abstract), indicating that no function has been assigned to these genes.

As mentioned above, the Appellant relies on sequence similarity (i.e. sequence homology) to conclude that all sequences similar to *ycf24* have similar function. However, as mentioned above, this method is not reliable. Another example indicating that sequence homology is an unreliable method for classifying genes, Denny (cited by the Appellants) teaches,

“A recent phylogenetic analysis of the apicomplexan plastid *tuf* gene (Kohler et al. 1997) placed it with green plastids rather than those of the red algae we originally suggested might be closest based on the then known distribution of ORF470 (*ycf 24*) (Williamson et al. 1994).” (See p. 56, second column).

Therefore, Denny clearly indicates that the original classification of *tuf* as a red algae gene based on sequence analysis alone was incorrect.

Regarding the function of *ycf24*, there is no indication in any of the cited references, nor in the prior art that any of the genes identified as *ycf24* genes have growth-associated functions. In fact, the cited references and the prior art do not indicate any specific function for the *ycf24* genes. Therefore, the association of the name “*ycf24* gene” appears to be based solely on sequence homology and there is no indication that all of the *ycf24* genes have growth-related function. Furthermore, there is no indication that the *ycf24* genes have any common specific structural elements which would confer a specific function to all *ycf24* gene products.

ycf24 Homologies:

Regarding Appellant’s argument that the “*ycf24* gene” has a highly conserved sequence across species, it is respectfully pointed out that sequence alignments of the three *ycf24* gene products disclosed in the specification show very limited sequence similarity (i.e. sequence homology). Sequence homology is determined by aligning sequences side-by-side and identifying the identical sequences. The sequence homology (i.e. amount of identical sequences)

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can be reported as “percent identity”. In the instant case, the *Plasmodium falciparum* ycf24 gene product (SEQ ID NO: 1) and the *Synechocystis* PCC6803 ycf24 gene product (SEQ ID NO: 2) are 42% identical at the amino acid level; the *Synechocystis* PCC6803 ycf24 gene product (SEQ ID NO: 2) and the *E. coli* ycf24 gene product (SEQ ID NO: 3) are 62% identical at the amino acid level; and the *Plasmodium Falciparum* ycf24 gene product (SEQ ID NO: 1) and the *E. coli* ycf24 gene product (SEQ ID NO: 3) are only 34% identical at the amino acid level (see attached sequence alignment). It is pointed out that the sequence identity between the *Plasmodium Falciparum* and *E. coli* ycf24 gene products is only 34%, well below the “~50%” identity that the specification suggests indicates that the gene products are likely to have the same general function. (See paragraph bridging pages 1-2 of the specification). Furthermore, considering that it is well known that a single nucleotide change can alter the function of a gene product (see sickle cell anemia above), one of skill in the art would not readily recognize gene products which are 34%, 42%, or 62% identical as necessarily having the same function; especially considering that the common attributes critical for function possessed by all the sequences have not been identified.

The ycf24 gene products have very limited sequence homology (based on the analysis above), and there are no identified functional elements or attributes common to all ycf24 gene products. For instance, there is no indication that all ycf24 gene products have any common functional domains. The specification does not disclose any structural limitations or requirements which provide guidance on the identification of sequences which meet the functional limitations. Therefore, although one of skill in the art might be able to recognize sequences which could be named “ycf24 gene products” based solely on sequence homology,

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one of ordinary skill in the art would not recognize that all of the “ycf24 gene products” had growth-associated function.

26 other ycf-34 genes identified in a public database:

The Appellant argues that a number of ycf24 genes and ycf24 gene products were known and identifiable at the time of the present invention, based on the identification of 26 different ycf24 genes identified in the NCBI public database. In response, it is respectfully pointed out that no essential features common to these 26 ycf24 gene products (or to any other ycf24 gene products) have been identified. Additionally, no specific function has been assigned to any of the 26 identified ycf24 gene products. It appears that the 26 ycf24s identified in the database were named “ycf24” based solely on a very limited sequence homology. It is reiterated that sequence homology alone, without identification of common structural or functional domains, cannot be indicative of the function of any gene or gene product.

Only Synechocystis PCC6803 and E. coli ycf24 have growth-associated functions:

The Appellant also contends that the specification exemplifies ycf24 genes by disclosing the sequence of SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3; and argues that the specification indicates that the ycf24 gene may be encoded by a polynucleotide which can selectively hybridize to the coding region of SEQ ID NO: 1, 2, or 3 (and indicate where in the specification examples of hybridization conditions are disclosed). Therefore, the Appellant contends, the present specification provides a functional and structural description of a number of ycf24 genes and ycf24 gene products. It is respectfully pointed out that the specification only

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indicates that the *Synechocystis* PCC6803 and *E. coli* ycf24 gene products (which have 62% identical amino acid sequences) have been explicitly disclosed in the specification as having growth-associated function. It is noted that the specification discloses that the *Synechocystis* PCC6803 and *E. coli* ycf24 gene products have growth-associated functions based on experiments where disrupting the ycf24 gene in these organisms was lethal. However, this showing only generically indicates that these two specific ycf24 genes are involved in the growth of these organisms. The experiment does not indicate any specific growth-associated function for these genes. There is no disclosure in the specification (or prior art) indicating any regions or domains of the *Synechocystis* or *E. coli* ycf24 gene product which are critical for their growth-associated function. Furthermore, there is no disclosure indicating any regions or domains which are common to all ycf24 gene products and which are critical to the growth-associated function of all ycf24 gene products.

Eli Lilly:

The Appellant also cites a number of decisions by the Federal Circuit, CCPA and other case law. For example, the Appellant cites *Eli Lilly* 119 F.3d at 1568, 43 USPQ2d at 1406, wherein the court found that claims involving generic formula usually indicate with specificity what the generic claims encompass. The issue before the *Eli Lilly* court was whether the generic statement “such as ‘vertebrate insulin cDNA’ or ‘mammalian insulin cDNA’, without more” is an adequate written description. In the *Eli Lilly* case the claimed genus encompassed species which had function but no structure. The *Eli Lilly* court found that such a generic recitation was not an adequate written description.

The instant application encompasses a claimed genus of species for which there are no disclosed specific structures and for which no specific functions have been associated. Specifically, the claims encompass any “ycf24 gene product”. All “ycf” gene products have been named “ycf” based solely on sequence homology as indicated by Kowallick (see above). However, no specific function has been assigned to any of the ycf24 genes in the prior art. Furthermore, the specification only indicates that the *Synechocystis* PC6803 and *E. coli* ycf24 gene products have a general growth-associated function. There is no indication that any other ycf24 gene products have growth-associated functions. Furthermore, the specification does not disclose any structural elements, such as functional domains, which are common to all ycf24 genes and which would indicate that the ycf24 genes had related functions. Additionally, considering that the sequences of the ycf24 gene products of *Plasmodium falciparum* and *E. coli* are only 34% identical, and considering that there are no disclosed common structural elements, one of skill in the art would not recognize that these two species of ycf24 gene products both possessed growth-associated functions.

Examples 14 and 18 of the Written Description Training Materials:

The Appellant also cites Examples 14 and 18 of the Written Description Training Materials in support of the arguments. Example 14 describes a claim drawn to a protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3, and that catalyze the reaction of $A \rightarrow B$. The analysis of the claim indicates that the variants of SEQ ID NO: 3 must possess the $A \rightarrow B$ catalytic activity and must have 95% sequence identity to SEQ ID NO: 3. In Example 14, the disclosure was determined to meet the written description

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requirement because the genus of variant sequences do not have substantial variation since all of the variants possess the specified catalytic activity and must have at least 95% sequence identity to the reference sequence. This differs from the instant case where the genus of ycf24 gene products are substantially variant, based on the definition of “ycf24 gene product” as, “generally [having] at least 50% sequence identity” to the reference sequence (See page 5, lines 17-25 of the specification). It is pointed out that the sequence identity between SEQ ID NO: 1, 2, and 3 (42%, 62% and 34%, as mentioned above) is much lower than the 95% given in Example 14.

Although Example 14 is similar to the instant case because the issue of both cases is the written description of a genus of variant sequences, the instant case is different from Example 14 because in the instant case the genus of ycf24 gene products can have substantial variation. Considering the claimed genus of ycf24 gene products can have substantial variation and considering that the disclosure does not identify the distinguishing attributes shared by all members of the genus, the instant disclosure does not provide sufficient written description of a representative number of ycf24 gene products.

Example 18 describes a claim drawn to a method of producing a protein of interest comprising obtaining *Neurospora crassa* mitochondria, transforming said mitochondria with an expression vector comprising a nucleic acid that encodes said protein of interest, expressing said protein of interest in said mitochondria and recovering said protein of interest. The Appellant indicates that the presently exemplified *Plasmodium*, *Synechocystis* and *E. coli* sequences, considered with the level of skill and knowledge in the art relating to ycf24 genes and gene identification, support the Appellant's belief that the specification provides an adequate written description of the claimed invention. However, Example 18 is irrelevant to the instant case

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because the issue of Example 18 is the written description of a genus of methods for making a protein in the mitochondria, while the issue of the instant case is the written description of a genus of different sequences. Therefore the issues of Example 18 and the instant case are not the same and, therefore, Example 18 is not relevant to the instant case. It is acknowledged that the presently exemplified *Plasmodium*, *Synechocystis* and *E. coli* ycf24 gene products can be made by several different well known methods.

Conclusion:

The claims encompass a method which comprises the use of any “ycf24 gene product”. Considering the broad definition of “ycf24 gene product” provided in the specification, it is clear that the claims encompass a genus comprising a huge number of “ycf24 gene products”. In order for the disclosure to meet the written description requirement, the disclosure must describe a representative number of species. A satisfactory disclosure of a ‘representative number’ depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by all members of the genus in view of the species disclosed. In the instant case, the disclosure has explicitly identified three specific species of the claimed genus (the *Plasmodium falciparum*, *Synechocystis* PC6803, and *E. coli* ycf24 gene products), but has not identified the necessary common attributes or features of the elements possessed by all members of the genus. Also, it is essential to the claimed method that all “ycf24 gene products” have a growth-associated function. Therefore, the specification must adequately describe the necessary common attributes and elements possessed by all members of the genus such that one of skill in the art could identify functional ycf24 gene products. However, the disclosure has not identified any common features which are essential to

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ycf24 gene product function. Therefore, the written description requirement has not been met and the rejection under 35 USC 112, first paragraph should be sustained.

Miscellaneous:

The Examiner wishes to thank the Appellant for pointing out the typographical error in Paper No. 22 which incorrectly indicated the "REPLY FILED 22 October 2002" has been considered. In fact, the Reply was filed 25 October 2002. Furthermore, the Examiner acknowledges consideration of the five references filed October 25, 2002, and has officially recognized the references by initialing the I.D.S (form PTO-1449) which is official Paper No. 20, submitted October 25, 2002 (attached).

For the above reasons, it is believed that the rejection should be sustained.


Respectfully submitted,

J. Eric Angell
Patent Examiner
Art Unit 1635

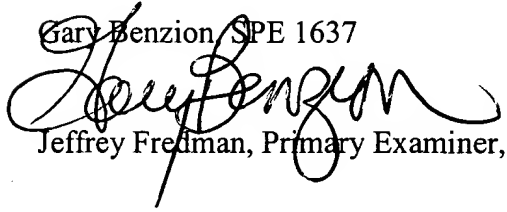
June 13, 2003

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SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Gary Benzion, SPE 1637


Jeffrey Friedman, Primary Examiner, 1634

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01 10 IntelliGenetics
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FastDB - Fast Pairwise Comparison of Sequences
Release 5.4

Results file lv2.res made by shanley on Thu 22 May 103 10:19:52-PDT

Query sequence being compared:	pep1_2 (1-480)
Number of sequences searched:	1
Number of scores above cutoff:	1

Results of the initial comparison of pep1_2 (1-480) with:
File : seq2toa.pep

Letter	Score
N	1
D	2
E	5
R	8
O	10
F	13
S	15
U	18

PARAMETERS

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Threshold level of sim.	6	30
Mismatch penalty	5.00	Joining penalty
Gap size penalty	0.33	Window size
Self score	0	
Randomization group	0	

SEARCH STATISTICS

Scores:	Mean	Median	Standard Deviation
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Times:      CPU      Total Elapsed
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Number of residues: 481
Number of sequences searched: 1
Number of scores above cutoff: 1

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The scores below are sorted by initial score. Significance is calculated based on initial score

A 100% identical sequence to the query sequence was not found

The 11st of best scores is:

Sequence Name	Description	Length	Score	Opt. Score	Sig.	Frame
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1. pep1_2 (1-480)
pep122_1 Sequence 2, Application US/09787633A

Initial Score	-	23	Optimized Score	-	323	Significance	-	0.00
Residue Identity	-	42%	Matches	-	205	Mismatches	-	223
Gaps	-	11	Conservative Substitutions	-			-	42

[illegible]

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| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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70      80      90      100      110      120      130

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210	220	230	240	250	260	270
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[illegible][illegible][illegible]

IntelliGenetics

FastDB - Fast Pairwise Comparison of Sequences
Release 5.4

Results file s.res made by shanley on Thu 103 12:45:23-PDT.

Query sequence being compared:	pep1221 (1-481)
Number of sequences searched:	1
Number of scores above cutoff:	1

Results of the initial comparison of pep1221 (1-481) with
File : pep1331g.pep

SCORE	STDEV
0	24
5	47
10	71
15	94
20	118
25	141
30	165
35	188
40	212

PARAMETERS

	PAM-150	K-tuple
Similarity matrix	16%	2
Threshold level of sim.		
Mismatch penalty	1	20
Gap penalty	1.00	Joining penalty
Size penalty	0.05	Window size
Coeff score	0	
Randomization group	0	

SEARCH STATISTICS

Scores:	Mean	Median	Standard Deviation
	212	0	0.00

```

Times:      CPU      Total Elapsed
           00:00:00.00  00:00:01.00

```

```

Number of residues: 509
Number of sequences searched: 1
Number of scores above cutoff: 1

```

The scores below are sorted by initial score. Significance is calculated based on initial score.

A1008 Identical sequence to the query sequence was not found

The list of best scores is:

Sequence Name	Description	Length	Score	Init. Opt.	Score	Sig.	Frame
SEA3 1. pep1331	TOIG of: pep133_1	check: 655	509	212	405	0.00	0

1. pep1221 (1-481)
pep1331 TOIG of: pep133_1 check: 6558 from: 1 to: 509

Initial Score	-	212	Optimized Score	-	405	Significance	-	0.00
Residue Identity	-	624	Matches	-	312	Mismatches	-	128
Gaps	-	23	Conservative Substitutions	-			-	37

3 → WKRLMGGGMSKNTEATDVKWTGGLPKYKEGFEQTOLATDELAKINEBVVAISAKRNEPEWMEFLRLN

AYRRWLMAEPTPAVHYPPIQDIIITYSAPQSK-----KIKESLEDPD-ALL-----ETEEKIGIPPI
 60 70 80 90 100 110
 AYRRWLMAEPTPAVHYPPIQDIIITYSAPQSK-----KIKESLEDPD-ALL-----ETEEKIGIPPI
 120 130 140

SEKRLRNVAVDLIPFSVSGTTEFKREKLAEVDYICSISEALOEHPDLQOKLTSSVPPLADNEFPALNNAVF
REG- -EVAVDLIPFSVSVAATYERKLEOGIFCSFCEAIHDPDELVRKTLGTVPGNNDFEALLNAAYAA
150 160 170 180 190 200 210

[illegible]

```

260      270      280      290      300      310      320      330
NADIKYSTVQVQVADGKSGKGYENFVKRLGKGVNSKISMTQVSGASATWKKYPSGVLTGDSVGEYSII
|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
NAEYKSYVQVQVFPD-NMFGILNFTYKRALCEGNSKMSWTQSEFGSATWKKYPSGLGDSNGISGEYSIV
290      300      310      320      330      340      350

```

ALTNKQADDTGKTHIKHGRNSTRISIKSGSAGNSYRGLVKPMKPGKAGANSOCDSMLTGDDAAANT

360 370 380 390 400

ALTSHQADDTGKTHIKHGRNTKTIIISKGSASHSONSTRGVLIMPTRYMANNFTQDSMLTGAACGATT

360 370 380 390 400 410 420 430

[illegible]

480
EGTVGX
| | | |
EHSV GX
X

> 0 <
01 10 Intelligenetics
> 0 <

FastDB - Fast Pairwise Comparison of Sequences
Release 5.4

Results file 143.res made by shanley on Thu 22 May 103 10:25:25-PDT.

Query sequence being compared: pep1_2 (1-480)
Number of sequences searched: 1
Number of scores above cutoff: 1

Results of the initial comparison of pep1_2 (1-480) with:
File: seq10aa.pep

100-
N 50-
B 50-
E 50-
R 50-
O 10-
S 5-
U 5-
E 5-
N 5-
C 5-
S 0-
SCORE 0 1 2 4 5 6 7 9 10 11
SIDEV

PARAMETERS

Similarity matrix PAM-150 K-tuple 2
Threshold level of sim. 100%
Mismatch penalty 6 Joining penalty 30
Gap penalty 5.00 Window size 480
Gap size penalty 0.33
Cutoff score 0
Randomization group 0

SEARCH STATISTICS

Scores: Mean Median Standard Deviation
11 0 0.00
Times: CPU 00:00:00.00 Total Elapsed 00:00:00.00

Number of residues: 509
Number of sequences searched: 1
Number of scores above cutoff: 1

The scores below are sorted by initial score.
Significance is calculated based on initial score.

* A 100% identical sequence to the query sequence was not found.

The list of best scores is:

Handwritten: SEARCH

Sequence Name	Description	Length	Score	Opt. Frame
1. pep133_1	Sequence 3, Application US/09	509	11	300 0.00 0

1. pep1_2 (1-480)
pep133_1 Sequence 3, Application US/09787633A
Initial Score = 11 Optimized Score = 300 Significance = 0.00
Residue Identity = 34% Matches = 165 Mismatches = 314
Gaps = 0 Conservative Substitutions = 0

3 → 1 → 10 → 20 → 30 → 40 → 50 → 60 → 70 → 80 → 90
TDDVKTMTGGLPLNKEGFFGTOLADELAKGNEEYVRAISAKRNEPEWLEPRLNAYRALEMEBPHTKAH

70 80 90 100 110 120 130
KYSKLNIIFKLPDMNPFDCPRINYNINIIYSSILKDNLIYKNNINIEFLDSIDIFDSMSI
YDKLNYODYSYISAPSCGNCDDTCASEPGAVOQGANAFLSKEVEAEQGLVYPRGEKAVDAIFDSYV

140 150 160 170 180 190 200
LHTQYFLKKGKGIIFLPEDIIKFKYLLIKKYLITIIISYKDNFANINSIIFSGFCYIPYVKCNFNLST
AATYREKLAEOGIIIFCSFGEALHDHPELVKRYLGTVPQNDNFALNANASDGTFTIYVPGVRCPEMLST

210 220 230 240 250 260 270
YFKTNSDPAQERFRLIIYVKYSYVSYLEGCTASLYKESOLHVAIVEIIVKDYGIKYITLQWYRGDYLG
YPRINAETGQEFRTILVADEDSYVSYIEGSCAPVRDSYQLAAVAEVIHKAAYKISTVQNMFGDNNTG

280 290 300 310 320 330 340 350
GGLYNFTTRGICLWNSKIDWLOVEGSIITWKYPSTILKGFISNFSISISMQIADTGSKYHIGSY
GILNFTYKRALCEGENSKMSWTQSETGSAITWKYIPSCILRGDINSIEFTSVALTSGHOADTGTAKIHIGKN

360 370 380 390 400 410 420
TKSYIISKSISLNSLNIIFRGVYIIPKFSKYNYVEGCSLFGNNSLWYTIPIYKINYNNTSYVKQEAFFSK
TKSTIISKISGHSNYSYRGVWKIMPTIYVARNFTQCSMLIGANGCAHTPTVECRNNSADLEHATTSR

430 440 450 460 470 480 490 500
IXEIVFLMORGLSISSESLIIGFCSDIYNKLPPEFNLEIPILFSLKIKDIFNXL
IGEDOLFYCLORGISSEDAISMIVNGFCQDVSELPLERAVEAKLLAISLEHSVX

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117-347

09/787,633

APPLICANT

WILSON et al.

FILING DATE

July 10, 2001

GROUP

1635

RECEIVED

OCT 30 2002

TECH CENTER 1600/2900

[illegible][illegible]

OTHER DOCUMENTS (including Author, Title, Date, Pertinent pages, etc.)			
11/1/02		Kowallik <i>et al</i> (1995) Plant Molecular Biology Reporter, 13, 336-342	
		Stirewalt <i>et al</i> (1995) Plant Molecular Biology Reporter, 13, 327-332	
		Douglas and Penny (1999) J. Mol. Evol. 48, 236-244	
		Reardon and Price (1995) Plant Molecular Biology Reporter, 13, 320-326	
11/6/02		Denny <i>et al</i> (1998) Protist, 149, 51-59	
Examiner		Date Considered	11/6/02

Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

Form PTO-FB-A820 (Also PTO-1449)